30.3

Novel strategy for chondral lesion repair in a goat model using an integrated hydrogel scaffold and marrow stimulation

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Purpose: We propose a novel strategy for chondral defect repair which utilizes a chondroitin sulfate adhesive and an integrated, injectable, in-situ polymerizable hydrogel scaffold used in conjunction with marrow stimulation. The purpose of this study was to evaluate the efficacy of this method in a goat model.
Methods and Materials: Surgery and analysis were performed with Good Laboratory Practices (GLP) and with IUACAC approval at Thomas Morris, Inc. in Reisterstown, Maryland. Two 6 mm chondral defects were created on the central ridge of the medial femoral condyle of the right stifle in caprine (goats, 2-3 years old). Experimental defects (n = 12, 6 goats)were primed with chondroitin sulfate ahesive and then microdrilled.Polyethelene glycol-hyaluronic acid-based hydrogel was applied as a liquid and then polymerized in defect by exposure to ultraviolet light. Control defects were left untreated (n = 6, 3 goats). Operative limb was immobilized for 2 weeks. Animals harvested at 6 months. Histological analysis included tissue fill, GAG staining, and blinded O'Driscoll scoring.
Results: Tissue fill was significantly greater in the scaffold treated defects, 77 % versus 66 % ($p < 0.05$). Safranin-O staining demonstrated significantly greater GAG content in scaffold treated defects, 53 % versus 34 %($p < 0.05$). O'Driscoll scoring was 17.7±2.9 for scaffold treated defects versus 14.8±3.5 for control defects.
Conclusions: Our method for cartilage lesion repair utilizing a scaffold and novel chondroitin sulfate adhesive demonstrated greater percent fill and GAG content and higher O'Driscoll scores than control defects. This study successfully establishes the feasibility of integrating in-situ polymerizable hydrogels into chondral lesions.

30.4

Experimental osteoarthritis in a stable knee joint using a critical size defect in an ovine model

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Purpose: Animal models simulating osteoarthritis are often associated with irreversible changes of the biomechanics- like ligament transection or meniscectomy. Although these models successfully induce osteoarthritis, the results of experimental repair procedures are impaired by the persistent biomechanics problem. The aim of this study is to define the critical size of a chondral lesion to induce osteoarthritis in a stable joint, allowing a more uninfluenced comparison of cartilage repair procedures.
Methods and Materials: 16 mature Austrian mountain sheep with a physiological joint status were divided randomly into four treatment groups. In each group a full thickness chondral cartilage defect was created in the weight bearing area of the right medial femoral condyle. The diameter of the defects was 7 or 14 millimetres. The sheep were fully weight bearing mobilized for six and twelve weeks. Osteoarthritis was determined by gross assessment, India-ink staining, biomechanical testing, histology (Mankin and OARSI Score) and immunohistochemestry for collagen type I and II. COMP was chronologically monitored by ELISA.
Results: In the six weeks group only minor osteoarthritis was detected in both defect sizes. After 12 weeks the seven millimetre defect created focal monocompartimental OA at the medial femoral condyle with minor degenerative changes at the corresponding tibia. The 14mm defect induced minor OA at the femoral condyle, but created major degenerative changes on the tibia.
Conclusions: A 7mm full thickness chondral defect with a weight bearing loading regime of 12 weeks can be considered as a suitable animal model to induce OA in otherwise stable joint.

30.5

Influence of matrix-based microfracture on the therapy of chondral defects in an animal model

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Purpose: Hyaline cartilage defects generally progress to osteoarthritis. Knutson et al. demonstrated that there is no benefit of ACT compared to microfracture for smaller defects. According to the hypothesis of the „causale histogenesis" of Pauwels mesenchymal stem cells have the potential to differentiate under mechanical stress to several tissues including hyaline cartilage. Aim of the present study was to improve cartilage defect repair by differentiation of adult mesenchymal stem cells with matrix based microfracture.
Methods and Materials: Two chondral defects (8mm diameter) were created in the weight-bearing area of the femur condyle of 12 sheep. The defects were either left untreated as control group, filled with matrix or were treated by microfracture or the combination of matrix and microfracturing. The animals were allowed full weight bearing after the operation. After 12 weeks the animals were scarified. Investigated parameters were: quantity and the quality of the regenerative tissue, evaluated by the score according to O`Driscoll and immune-histochemistry for Aggrecan, Collagen I and II.
Results: The results of all treated groups showed significant higher tissue regeneration compared to the untreated controls. Only the matrix based microfracture showed a significant improved result in the score according to Oâ€™Driscoll. (void: 8,3 points, mircrofracture 8,8 points, matrix 12,5 points, matrix based mircrofracture 20,8 points. This tissue shows hyaline like orientation.
Conclusions: In our present animal model, the combination of matrix with microfracture appears to be superior to clinically established microfracture.

30.6

An in-vivo mouse model for human cartilage repair

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Purpose: Cartilage regeneration methods have been examined in animal models with animal cells. The major limitation of those studies is the biological difference in human and animal cartilage. We propose an in-vivo model of human chondrocytes in a human cartilage defect environment.
Methods and Materials: Human full-thickness (2-4mm) articular cartilage discs, 10mm in diameter and attached to 3-6mm of subchondral bone, were obtained from human femur heads upon joint replacement. Chondral defects (4mm diameter) were set without violating the subchondral bone. Human chondrocytes were isolated and cultivated for up to 3 passages and then suspended in a concentration of 10^7 cells/ml. The defect was completely filled with the cell suspension (~30µl) and cells were allowed to adhere to the cartilage inner surface for 45 minutes. Defects were covered with a thin sheet of human periosteum, fixed with a drop of fibrin sealant. Discs were implanted subcutaneously in the back of nude mouse for either 5 or 8 weeks.
Results: Histological evaluation revealed a gradient of differentiation from the cartilage lateral side to the center of the defect. A proteoglycane rich matrix (Alcian Blue positive) was formed with chondron-like structures. After 8 weeks, the areas of differentiating cells had enlarged in comparison to 5 weeks, implementing a progress of cartilage repair. Discs implanted without cells or cover showed no chondrogenesis.
Conclusions: The introduced model is a promising new in vivo model to study human cell behavior in a human cartilage defect environment, with the limitation of lacking synovial fluid and mechanical loading.